REMARKS

Claims 66-99 were pending in the present application. Applicants have hereinabove canceled claims 69 and 85, without prejudice to refiling these claims in a future application that claims the benefit of the subject application's filing date under 35 U.S.C. § 120, and amended claims 66-68 and 84. Claims 71, 74-78, 81, 87, 90-94, and 97 have been withdrawn from consideration pending the allowance of a generic claim that embraces the species claimed. Accordingly, claims 66-68, 70-84, and 86-99 are pending in the present application, and claims 66-68, 70, 72, 73, 79, 80, 82-84, 86, 88, 89, 95, 96, 98, and 99 are under consideration at this time.

The Office Action stated "*claims reading on the second species (e.g. DNA encoding 75 kD receptor fusion protein) were not even presented in the instant application until the amendment filed 8/31/2000*" [emphasis in original text]. This is incorrect. Claims 66 and 67, filed in an Amendment dated August 22, 1996, generically claim DNA that encodes for a 75 kD fusion protein, i.e. DNA encoding a chimeric polypeptide comprising the extracellular domain of a TNF receptor polypeptide functionally attached to a Fc portion and hinge region of an IgG heavy chain polypeptide.

Since the restriction requirement appears to have been made final based on an erroneous underlying assumption, reconsideration of the finality of the restriction requirement is earnestly solicited. In addition, applicants reserve their right to petition this restriction requirement.

Claims 66-70, 72, 73, 79, 80, 82-86, 88, 89, 95, 96, 98, and 99 were rejected under 35 U.S.C. § 112, first paragraph.

Claims 66 and 67 were alleged to encompass the nucleic acids encoding any extracellular domain of a TNF receptor from any species. In response, applicants have amended these claims to recite "the extracellular domain of an insoluble human TNF receptor polypeptide having an apparent molecular weight of about (a) 55 kilodaltons or (b) 75 kilodaltons on a non-reducing SDS-polyacrylamide gel." Such claims are fully supported by the specification and comply with 35 U.S.C. § 112, first paragraph.

Claims 68, 72, 73, and 84 were alleged to encompass nucleic acids encoding soluble portions of insoluble TNF binding proteins irregardless [sic.] of the molecular weight of said receptors (binding protein and receptor appear to be used interchangeably by the Patent Office). In response, applicants have amended these claims to recite that the "DNA subsequence encodes the soluble portion of an insoluble human tumor necrosis factor binding protein having an apparent molecular weight of about (a) 55 kilodaltons or (b) 75 kilodaltons on a non-reducing SDS-polyacrylamide gel." Such claims are fully supported by the specification and comply with 35 U.S.C. § 112, first paragraph.

The Patent Office drew attention to *The Regents of the University of California v. Eli Lilly and Company* cases for the proposition that the description of a single species of cDNA encoding rat insulin does not meet the description requirement for a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans.

Contrary to the position set forth in the Office Action, applicants' claimed invention meets the description requirement as set forth in the mentioned cases. Applicants' claimed invention relates to DNA encoding the soluble portion of an insoluble **human** tumor necrosis factor binding protein having an apparent molecular weight of about **(a)**

55 kilodaltons or (b) 75 kilodaltons on a non-reducing SDS-polyacrylamide gel. Thus, unlike the situation in *The Regents of the University of California v. Eli Lilly and Company* cases, there is no ambiguity as to what is being claimed by applicants. Applicants have provided a written description of the invention an the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the are to which it pertains, or with which it is most nearly connected, to make and use the same.

In view of the above, applicants request that all rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 66-70, 72, 79, 80, 82, 84-86, 88, 95, 96, and 98 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Schall et al. [Cell, 61: 362-370 (1990)] in view of Capon et al. (U.S. Patent No. 5,428,130).

In the Office Action it is stated that it

> "would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Schall et al. teach the nucleic acid sequence encoding an insoluble (e.g. membrane bound) 55kD TNF receptor while Capon et al. teach DNA encoding soluble Ig/ligand binding fusion proteins wherein the ligand binding protein is a soluble portion derived from a cell surface receptor. One of ordinary skill in the art would have been motivated to do the aforementioned because Capon et al. teach that the ligand binding portion of the Ig/ligand binding fusion protein can be derived from a wide variety of different known cell surface receptors (see column 7, third paragraph from the bottom) and that said fusion proteins have a variety of a uses (see column 4) [printed as written in the Office Action]."

Schall et al. has an apparent publication date of April 20, 1990. Applicants have claimed priority under 35 U.S.C. § 119 from three Swiss patent applications, including Swiss Patent Application No. 746/90, filed on March 8, 1990. Figure 1 of this priority application sets forth the cDNA sequence of the p55 TNF binding protein and predates Schall et al. An English translation of this priority application may be found in related application, Application No. 08/444,793 (now U.S. Patent No. 5,808,029). There is no relevant disclosure in Schall et al. that extends beyond that which was already taught in applicants' mentioned priority application.

Capon et al. discloses hybrid immunoglobulins. However, there is no teaching or suggestion in Capon et al. to create a hybrid immunoglobulin using TNF binding proteins or TNF receptor proteins. The only hybrid immunoglobulins actually made by Capon et al. incorporate CD4 (a member of the immunoglobulin gene superfamily) and MLHR (murine lymphocyte homing receptor, i.e. a lymphocyte cell surface glycoprotein). Even though Capon et al. discloses a laundry list of ligand binding partners, there is no suggestion to use TNF. Therefore, one of ordinary skill in the art would not have been motivated to make a TNF-containing hybrid immunoglobulin based on the disclosure of Capon et al.

Likewise, Schall et al. provides no motivation to create a hybrid immunoglobulin since immunoglobulins are not even mentioned. Therefore, neither Capon et al. nor Schall et al. provides any motivation to search for a polynucleotide which comprises two DNA subsequences, one encoding an insoluble protein which is capable of binding human tumor necrosis factor, and the other encoding all of the domains of the constant region of the heavy chain of a human immunoglobulin other than the first domain of the constant region.

The Patent Office has generated the type of piece-meal hindsight analysis that is consistently shunned by courts. Schall et al. would not have lead one of ordinary skill in the art to Capon et al. and Capon et al. would not have lead one of ordinary skill in the art to Schall et al. There is simply no nexus found in these documents that would have lead one of ordinary skill in the art to combine these two disclosures.

In summary, there is no motivation to combine Schall et al. and Capon et al., nor is there any guidance in these two documents that would lead one of ordinary skill of the art to applicants' claimed invention. Moreover, there is no teaching or suggestion that applicants' claimed compounds would be superior to the soluble receptor protein itself.

In view of the above, applicants request that all rejections under 35 U.S.C. §103 be withdrawn.

Applicants request reconsideration, withdrawal of all rejections under 35 U.S.C. §§ 112 and 103, and the issuance of a Notice of Allowance.

No fee, other than the fee for a three-month extension of time, is required in connection with the filing of this Amendment. If any fee is deemed necessary,

authorization is hereby given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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TEXT MARKED TO SHOW CHANGES MADE

-- 66. (Amended) A DNA segment having a sequence encoding a chimeric polypeptide comprising the extracellular domain of ~~a~~ an insoluble human TNF receptor polypeptide having an apparent molecular weight of about (a) 55 kilodaltons or (b) 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, functionally attached to a Fc portion and hinge region of an IgG heavy chain polypeptide. --

-- 67. (Amended) A recombinant vector incorporating a DNA segment having a sequence encoding a chimeric polypeptide comprising the extracellular domain of ~~a~~ an insoluble human TNF receptor polypeptide having an apparent molecular weight of about (a) 55 kilodaltons or (b) 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, functionally attached to a Fc portion and hinge region of an IgG heavy chain polypeptide. –

-- 68. (Amended) A DNA sequence which encodes a chimeric protein and comprises (i) a first DNA subsequence joined to (ii) a second DNA subsequence, wherein the first DNA subsequence encodes the soluble portion of an insoluble human tumor necrosis factor binding protein having an apparent molecular weight of about (a) 55 kilodaltons or (b) 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, wherein the soluble portion is capable of binding to human tumor necrosis factor, and wherein the second DNA subsequence encodes all of the domains, other than the first domain, of the constant region of the heavy chain of a human immunoglobulin. --

-- 84. (Amended) A DNA encoding a chimeric protein prepared by a process which comprises joining a first DNA subsequence to a second DNA subsequence,

wherein the first DNA subsequence encodes the soluble portion of an insoluble human tumor necrosis factor, binding protein having an apparent molecular weight of about (a) 55 kilodaltons or (b) 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, wherein the soluble portion is capable of binding to human tumor necrosis factor and wherein the second DNA subsequence encodes all of the domains, other than the first domain, of the constant region of the heavy chain of a human immunoglobulin. --